

**IN THE CLAIMS**

Please replace all prior versions, and listings, of claims in the application with the following list of claims. Additions are indicated by underlining and deletions are indicated by strikeouts and/or double bracketing.

1-44. (Cancelled)

45. (Currently Amended) In a method of producing a device comprising a predetermined reaction site having a volume of less than ~~[[1]]~~ 2 ml, the improvement comprising:  
attaching a first component of the device to a second component of the device with or without auxiliary adhesive to produce a portion of the device that defines the predetermined reaction site.
46. (Original) The method of claim 45, wherein the predetermined reaction site is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
47. (Original) The method of claim 45, wherein the improvement comprises sonic welding the first component to the second component.
48. (Original) The method of claim 45, wherein the improvement comprises heat pressing the first component to the second component.
49. (Currently Amended) The method of claim 45, wherein the first component comprises at least one polymer selected from the group consisting of polycarbonate, polysulfone, polyethylene, polystyrene, and blends and copolymers thereof.
50. (Original) The method of claim 45, wherein the improvement comprises applying energy to melt at least a portion of the first component.

51. (Original) The method of claim 50, wherein the energy comprises ultrasound.
52. (Original) The method of claim 50, wherein the energy comprises heat energy.
53. (Original) The method of claim 45, wherein the improvement comprises attaching the first component to the second component to produce a liquid-tight junction therebetween.
54. (Previously Presented) The method of claim 45, wherein the device is enclosed.
- 55-56. (Cancelled)
57. (Currently Amended) An apparatus, comprising:  
a predetermined reaction site having a volume of less than about  $[[1]] \geq 2$  ml,  
constructed and arranged to carry out a chemical or biological reaction promoted by or  
monitored by electromagnetic radiation within a predetermined wavelength range; and  
a membrane, transparent to electromagnetic radiation within the predetermined  
wavelength range in the infrared to ultraviolet range to the extent necessary to promote or  
monitor the reaction, having a pore size of less than 2.0 microns in fluid communication  
with the predetermined reaction site.
58. (Original) The apparatus of claim 57, wherein the predetermined reaction site is constructed  
and arranged to maintain at least one living cell at the predetermined reaction site.
59. (Original) The apparatus of claim 57, wherein the membrane is substantially transparent to  
incident visible electromagnetic radiation.
60. (Original) The apparatus of claim 57, wherein the membrane is substantially transparent to  
incident electromagnetic radiation having a wavelength of between about 400 nm and about  
800 nm.

61-65. (Cancelled)

66. (Currently Amended) An apparatus, comprising:

a device comprising a first predetermined reaction site having a volume of less than about  $[[1]]$  2 ml and a second predetermined reaction site, the device defining a pathway fluidly connecting the first predetermined reaction site and the second predetermined reaction site, wherein the pathway crosses a membrane.

67. (Original) The apparatus of claim 66, wherein the first predetermined reaction site is constructed and arranged to maintain at least one living cell at the first predetermined reaction site.

68. (Previously Presented) The apparatus of claim 66, wherein the device is enclosed.

69. (Cancelled)

70. (Currently Amended) The apparatus of claim 66, wherein the second predetermined reaction site has a volume of less than about  $[[1]]$  2 ml.

71-78. (Cancelled)

79. (Original) An apparatus, comprising:

a reaction site having a first portion and a second portion separated by a membrane;  
and

at least a first and a second channel in fluidic communication with the second portion of the reaction site.

80. (Original) The apparatus of claim 79, wherein the reaction site has a volume of less than 2000 microliters.
81. (Original) The apparatus of claim 79, wherein the reaction site has a volume of less than 1000 microliters.
82. (Cancelled)
83. (Original) The apparatus of claim 79, wherein the membrane comprises at least one of polycarbonate, cellulose, nitrocellulose, glass, fiberglass, or polycarbonate, regenerated cellulose, or polyethylene.
- 84-85. (Cancelled)
86. (Original) The apparatus of claim 79, wherein the membrane has a pore size less than 10 microns.
- 87-89. (Cancelled)
90. (Original) The apparatus of claim 79, wherein the second portion of the reaction site is coated with a cytophilic material.
91. (Original) The apparatus of claim 79, wherein the first portion of the reaction site comprises a cytophilic material.
92. (Cancelled)
93. (Original) The apparatus of claim 79, further comprising a pH sensor in sensing communication with the reaction site.

94. (Cancelled)

95. (Original) The apparatus of claim 79, further comprising an optical density sensor in sensing communication with the reaction site.

96. (Original) The apparatus of claim 79, further comprising a glucose sensor in sensing communication with the reaction site.

97-101. (Cancelled)

102. (Previously Presented) The apparatus of claim 79, wherein the membrane is substantially impermeable to animal cells.

103-105. (Cancelled)

106. (Original) A method, comprising:

providing a substrate having a surface into which is fabricated a plurality of reaction sites, at least one reaction site having a volume less than about 2 ml and divided by a substantially cell impermeable membrane into at least a cell culture portion containing cells and a reservoir portion not containing cells, the reservoir portion being fluidly connected to at least a first and a second channel fabricated into the surface of the substrate;

introducing at least one test compound into at least one of the plurality of reaction sites; and

monitoring the effect of the at least one test compound on cells located within the cell culture portion.

107. (Original) The method of claim 106, wherein the membrane allows waste products produced by the cells to enter the reservoir portion.

- 108. (Original) The method of claim 106, wherein the membrane allows a protein produced by the cells to enter the reservoir portion.
- 109. (Cancelled)
- 110. (Original) The method of claim 106, wherein the contents of the reservoir portion is periodically replaced during at least a first period of time.
- 111. (Cancelled)
- 112. (Original) The method of claim 106, wherein the cells include eukaryotic cells.
- 113-114. (Cancelled)
- 115. (Original) The method of claim 106, wherein the step of monitoring comprises measuring a fluorescent signal influenced by the at least one test compound.
- 116. (Original) The method of claim 106, wherein the cell culture portion comprises a first type of cell and a second type of cell.
- 117. (Cancelled)
- 118. (Previously Presented) The apparatus of claim 79, wherein the substrate is formed from a copolymer.
- 119. (Previously Presented) The apparatus of claim 79, further comprising an oxygen sensor in sensing communication with the reaction site.